ALBERTA HERITAGE FOUNDATION FOR MEDICAL RESEARCH

ahfmr research news

SPRING 2003

New tools in the fight against cancer

On the Cover

Ladybug

"Ladybugs defy what my dad calls "The Laws of Physics" because they fly but supposedly that isn't possible. People with cancer become like ladybugs because many of them defy the seemingly impossible odds so their mind, body, and spirit can fly in their own way, no matter how many obstacles cancer puts in their way."

– Allison Brett

Allison created the tile photographed on the front cover during the time her mother was in the hospital. Allison participated in the Revlon "Arts in Medicine" Programme at the Cross Cancer Institute in Edmonton.

research news

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AHFMR Mission

AHFMR supports a community of researchers who generate knowledge that improves the health and quality of life of Albertans and people throughout the world. AHFMR's long-term commitment is to fund basic, patient and health research based on international standards of excellence and carried out by new and established investigators and researchers in training.

Contact Us:

Your comments, views and suggestions are welcome. Please forward them to:

The Editor, AHFMR Research News
Alberta Heritage Foundation
for Medical Research
Suite 1500,
10104 - 103 Avenue
Edmonton, Alberta T5J 4A7

Phone: (780) 423-5727
Fax: (780) 429-3509
E-Mail: ahfmrinfo@ahfmr.ab.ca
Internet: www.ahfmr.ab.ca

AHFMR
ALBERTA HERITAGE FOUNDATION FOR MEDICAL RESEARCH

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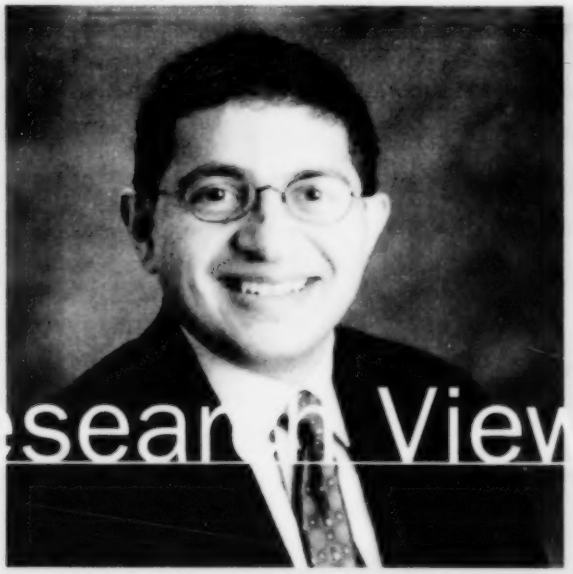

"That AHFMR Studentship gave me my first exposure to research," says Dr. Husain. He explains that he enjoyed his genetics course with the University of Calgary's Dr. Michael Bentley (himself a recipient of AHFMR Independent Establishment funding) so much that he approached him about how to do research in the area. Dr. Bentley directed him to AHFMR, then a fledgling funding agency in only its third year of operation. "That intensive summer of research was obviously a good experience–it kept me coming back."

Dr. Husain graduated from medical school at the University of Alberta in 1986 as the gold medallist in his class. "I was very lucky to have such positive role models at the U of A, who were very influential in what I would eventually do" he explains. That turned out to be a return to research in the form of a post-doctoral fellowship in cardiovascular molecular biology at MIT (Massachusetts Institute of Technology) as a CIHR (Canadian Institutes of Health Research) Clinician-Scientist trainee.

Now a clinician-researcher and cardiologist in Toronto, Dr. Husain treats many patients with coronary artery disease. His research focuses on the molecular processes governing smooth-muscle cell growth in arteries, and the responses of heart muscle to injury. In 2002, his research lab discovered that the iNOS (inducible nitric oxide synthase) enzyme–a gene involved in the body's immune response–causes heart rhythm problems when over-expressed. More recently, his work has developed a novel approach to blocking smooth-muscle cell growth after angioplasty.

Dr. Husain finds that the demands of his medical practice often make it impossible to devote more than 75% of his time to research. "If you see a patient on one day, you then have to answer calls and look up lab results and test results, write letters, and review charts. There's just no way you can do medicine only one day a week."

Dr. Husain also continues to share his expertise and give something back to the research community by sitting on a number of scientific committees. In addition to his work with AHFMR, he has been a member of scientific review committees for CIHR and the Heart and Stroke Foundation of Canada. "But serving on the AHFMR committee has the added benefit of bringing me back to Alberta once in a while so I can visit my parents," he says with a smile.

Dr. Mansoor Husain is a member of AHFMR's Clinical Committee. He is a research scientist at the Toronto General Hospital Research Institute, in the Division of Cellular and Molecular Biology. He is also the associate director of the Coronary Intensive Care Unit at the Toronto General Hospital and an Assistant Professor in the University of Toronto's Department of Medicine.

Closing the gate on pain

Pain is a necessary part of life. It can warn us that we're hurt and protect us from further injury. But sometimes it hurts to the point of being unbearable.

Dr. Gerald Zamponi is helping design a new type of painkiller for very severe pain, such as that following surgery or related to cancer. He believes this new pill will be a major breakthrough, because it will block pain as effectively as existing painkillers but without the side effects associated with drugs such as morphine.

"This pill will not be for your average everyday headache," Dr. Zamponi explains. "It will be for people who are on all sorts of pain medications that are ineffective for them."

Calcium plays a number of extremely important roles in the body.

The new drug will target calcium channels in order to treat pain. Calcium plays a number of extremely important roles in the body, including ensuring that the brain and heart function correctly. In the brain, calcium entering nerve cells controls nerve-to-nerve communication. In the heart, calcium is responsible for the contraction of heart muscle.

Yet too much calcium is toxic. The amount of calcium entering brain and heart cells must be precisely controlled. Calcium channels let calcium into your brain cells and let it back out again, explains Dr. Zamponi. Different calcium channels are responsible for different things in each nerve cell. Some are linked to gene expression. Some are linked to nerve communication. Others are related to how excitable a nerve cell is and how well it conducts electricity. Calcium channels open, close, and become inactive in response to electrical nerve signals.

Dr. Zamponi and his colleagues are closely examining how calcium channels work and how they are regulated, in order to better understand what happens in certain health problems. He is particularly interested in developing drugs that will directly block the channels and thus block pain. His lab is also investigating new ways to treat schizophrenia through targeting calcium channels.

The new pain medication has already been found to be "spectacularly" successful in treating pain in research studies involving animals, according to Dr. Zamponi. The next step will be to test it in Phase 1 clinical trials in humans, likely later this year in the United States. This work is being carried out through Dr. Zamponi's involvement with Vancouver biotech company NeuroMed Technologies. Dr. Zamponi was involved in the original drug design and testing, and continues to contribute his expertise to NeuroMed's drug development program to help make this treatment available to the public.

Dr. Zamponi's research on calcium channels is not only fundamental to NeuroMed's work on pain, but also highly relevant to several other conditions. Mutations of calcium channels have been identified as factors in some genetic disorders, such as migraine, epilepsy, and night blindness. Someday, new drugs will be developed that treat epileptic seizures, pain, and stroke damage by targeting these mutated channels.

Dr. Gerald Zamponi is an Associate Professor in the Department of Physiology and Biophysics, and the Novartis Chair for Schizophrenia Research at the University of Calgary. He is a Heritage Senior Scholar and a Canadian Institutes of Health Research Investigator.

Selected publication

Jarvis SE, Barr W, Feng Z-P, Hamid J, Zamponi GW. Molecular determinants of syntaxin 1 modulation of N-type calcium channels. *Journal of Biological Chemistry* 2002 Nov 15; 277(46):44399-44407.

RIGHT: DR. GERALD ZAMPONI

Disease-causing viruses are adept copycats. But Heritage Medical Scholar Dr. Kenneth Ng is getting closer to shutting down their infectious act.

Eliminating copycats

Dr. Gerald Zamponi is helping design a new type of painkiller for very severe pain.

There are thousands of viruses, from the rhinovirus that causes the common cold to the HIV virus responsible for life-threatening AIDS. Dr. Ng wants to understand the molecular structure of a large class of infectious particles called positive, single-strand RNA viruses. This notorious family includes the viruses that cause disabling polio and liver disease in people, and often-fatal foot-and-mouth disease in cattle and pigs. Other viruses in this family making front-page news these days are the dangerous West Nile virus, spread by mosquitoes, and severe acute respiratory syndrome (SARS).

"For all of these viruses, the big problem is that if you get infected by them and you don't have immunity, then you'll come down with a disease for which there's no effective treatment," says Dr. Ng.

The members of this viral family have a genome consisting of just one strand of a protein called RNA (ribonucleic acid). (A genome carries an organism's genes, which is its coded genetic makeup.) RNA helps interpret this code so a cell can produce the proteins it needs for its normal activities, including making more cells. "For the infection process to occur, the virus has to bind to the outside of the cell, and then has to inject its genome into the cell," explains Dr. Ng. Once inside the cell, the viral RNA strand mimics the RNA naturally present in the cell. It signals the cell to start making viral proteins which the virus needs in order to copy itself and spread the infection.

To study how the single-strand RNA virus "tricks" the cell, Dr. Ng studies non-infectious protein components of an animal model of the virus. He focuses on one of the virus's most important enzymes, RNA polymerase. The polymerase's job is to take the one strand

RIGHT: DR. KENNETH NG

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Eliminating copycats

of viral RNA that first infects a cell and make a new "negative" strand—so called because it is complementary to the original, positive strand. Using this copycat piece of viral genetic material, polymerase can then churn out hundreds of new genomes to infect more cells. Dr. Ng uses a technique called x-ray crystallography to peer into the molecular structure of polymerase. To reveal the atom-by-atom structure, he directs a high-energy x-ray beam at microscopic-sized crystals made from purified samples of the viral enzyme.

Over the last two years, Dr. Ng and his research collaborators became the first in the world to figure out the entire structure of the rabbit virus polymerase. They have also identified the active sites of the chemical reaction by which the polymerase makes new viral genomes.

Dr. Ng's next step is to find an inhibitor, a chemical substance that blocks polymerase's function in the rabbit virus. If successful, the technique should work against all the other disease-causing members of the viral family in which the enzyme acts the same way. "The idea is to develop a drug that stops this enzyme, this part of the cycle. If you're able to stop polymerase, then you're able to stop the virus."

Dr. Ng is a Heritage Medical Scholar who also receives funding from the Canadian Institutes of Health Research (CIHR).

Selected publications

Wang M, Ng KKS, Cherney MM, Chan L, Yannopoulos CG, Bedard J, Morin N, Nguyen-Ba N, Alaoui-Ismaili MH, Bethell RC, James MNG. Non-nucleoside analogue inhibitors bind to an allosteric site on HCV NS5B polymerase: crystal structures and mechanism of inhibition. *Journal of Biological Chemistry* 2003 Mar 14;78(11):9489-9495.

Barrette-Ng IH, Ng KKS, Mark BL, van Aken D, Cherney MM, Garen C, Kolodenko Y, Gorbalenya AE, Snijder EJ, James MNG. Structure of arterivirus nsp4. *Journal of Biological Chemistry* 2002 Oct 18;277(42): 39960-39966.

Ng KKS, Cherney MM, Vázquerz AL, Machín A, Alonso JMM, Parra F, James MNG. Crystal structures of active and inactive conformations of a caliciviral RNA-dependent RNA polymerase. *Journal of Biological Chemistry* 2002 Jan 11;277(2):1381-1387.

ABOVE: DR. KENNETH NG

Bio

Alex McPherson jokingly refers to himself as the "old codger" of Canadian biotechnology. With 12 years as CEO of Biomira Inc., Dr. McPherson is the longest-continuously-serving biotech CEO in Canada. This might not be a notably long tenure in many industries; but in the volatile world of biotechnology, where CEOs stay an average of 3 to 6 years, 12 years seems close to a lifetime. In that time Dr. McPherson has learned a lot, not just about Biomira but about the ingredients for success in biotech.

"Biotech is a very volatile, high-risk, speculative growth enterprise," he says. "The environment is opposite to everything that research needs, which includes consistency, stability, and predictability. And yet biotech enterprises are intimately connected to research. It's where their ideas, their innovation comes from. You absolutely must have very good foundation science."

However, a biotechnology company is not a university research lab in disguise, notes Dr. McPherson. "Biomira was founded in 1985 by University of Alberta researchers, and during its early days the company relied on U of A facilities. The linkages were very close. But as we've grown, that connection has become much less evident.

"I believe this shift has to happen in every biotech start-up company. There has to be a genuine, in some cases traumatic move from a quasi-academic base to an industry focus.

We don't spend huge amounts on discovery research. We're focused on products."

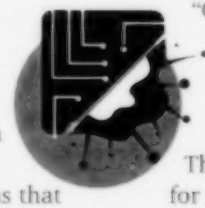
One of those products is Theratope cancer vaccine. Final data analysis of the Phase 3 clinical trial of Theratope vaccine in women with metastatic breast cancer is expected in mid-2003. If the results are positive, Biomira and its partner, the German pharmaceutical company Merck KGaA, will begin the process of filing for

tech

"Biotech is a very volatile, high-risk, speculative growth enterprise."

The fire in the belly

regulatory approval. Theratope is one of Biomira's two lead product candidates, the other being BLP25 Liposomal vaccine, which is also a potential cancer therapy. It is currently in Phase 2 trials.



This brief summary masks the incredible complexity involved in turning scientific research into viable products. Dr. McPherson says Biomira's history is typical of biotech start-ups. "Companies tend to start with ideas that are way too big, and consequently their ability to attract investors is almost nil. Gradually, though, companies become more focused. This is what happened at Biomira. We had to make hard decisions about what potential products to concentrate on.

"Biotech companies tend to take this hourglass shape—wide at the top in the early days, then narrowing down, and eventually widening again as they expand their product pipeline. But it's a very tough business. Commercialization is incredibly difficult. Many companies simply disappear when they get to the skinny part of the hourglass."

Besides having good foundation science and being able to make the transition from academia to business, Dr. McPherson credits Biomira's success to very patient venture capital from Altamira, one of Canada's largest venture capital investors. "Altamira stuck with our company when they could have exited. We wouldn't have been able to progress the way we have without them."

Finding the right management expertise is also a challenge for start-up companies. "There's a pool of competent people in Canada; however, they're all employed and we're not adding to the pool. It is very hard to attract people here—we don't offer the salaries or the tax advantages of countries like the US. The quality of life we enjoy in Alberta can be an important factor in attracting people here, but it's a soft issue and hard to quantify."

What about researchers running their own companies? That can work, says Dr. McPherson, except that the skills needed at start-up are not the same ones required when the company becomes established.

"Once you get to a certain level, you become a bureaucrat. You have to be process-oriented. There are a lot of people who can start a company but can't run one, and vice versa.

"Having the right people with you is vital. The most dangerous person to have working for you is the person who doesn't know what he doesn't know. He's on the learning curve on your money."

While science, financing, and management skills are all part of a recipe for success in biotech, Dr. McPherson says there is one ingredient that no start-up can do without: heart. "At the end of the day, it's up to the researcher whether he or she wants to become an entrepreneur. You have to have a fire in your belly to do this—it's an awful lot easier to be an academic. You'll never be as rich, but you'll never risk poverty. Most entrepreneurs have made serious personal investments in their enterprises. Some win and some lose. That's the reality...and that's the thrill."

The SEARCH

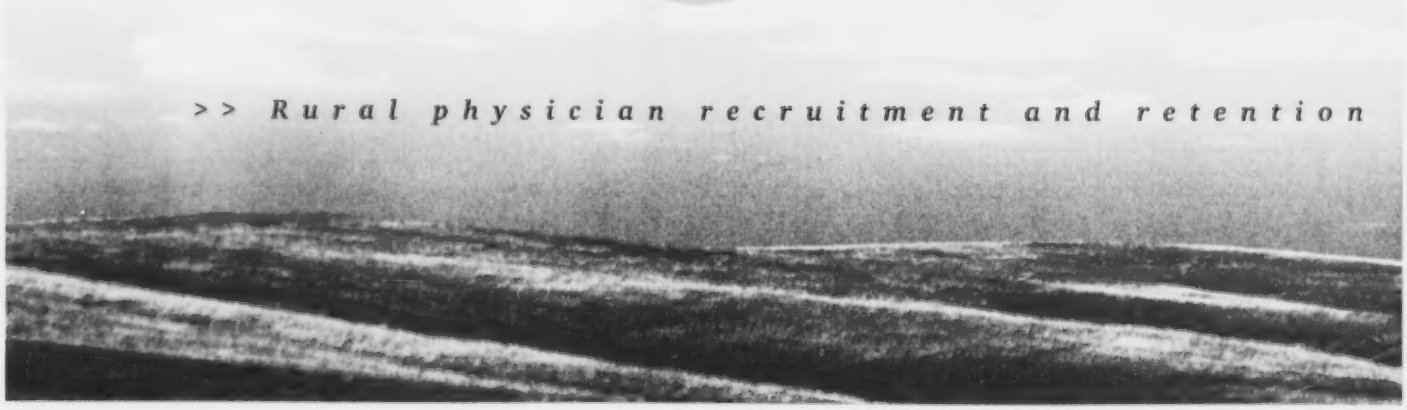
Remember Dr. McCoy from the Star Trek television series? According to Sundre physician Dr. Carol Rowntree, "Bones" McCoy had all the qualities necessary to be a doctor in a small, rural community–qualities like a sense of adventure, a broad range of skills and knowledge (since he worked far from a tertiary care center), the ability to work independently in emergency situations, and commitment to his community and his profession.

So where are Alberta's Dr. McCoys?

Rural physician recruitment and retention has long been an issue in Alberta and across the country. The Canadian Medical Association has estimated that rural areas of Canada are short more than 1600 physicians. Through the Alberta Heritage Foundation for Medical Research, Dr. Rowntree has undertaken a research project to help increase recruitment to rural areas by identifying medical students with interests and characteristics making them likely to choose rural careers. She is conducting the study through the SEARCH (Swift Efficient Application of Research in Community Health) program. SEARCH is an AHFMR initiative that improves regional research capacity across Alberta by training healthcare professionals to conduct and assess applied health research.

Working in conjunction with Dr. Bruce Wright, director of Admissions and Student Affairs at the University of Calgary's Faculty of Medicine, Dr. Rowntree administered a questionnaire in August 2002 to incoming medical students at that university. The goal was to identify students with interest in rural medicine based on information gleaned from previous studies of rural practitioners. The most important factors were previous exposure to rural life, experience with some kind of overseas work, a history of volunteerism or community work, and an interest in practising family medicine. "A lot of the American literature suggests that older males are more likely to go into rural medicine, but age and gender do not appear to be important factors in Australia and Canada," Dr. Rowntree adds.

The next step in the project was to recruit rural faculty advisors to match with those students identified as having an interest in rural medicine. When students enter Medicine at the U of C, they are each assigned a faculty advisor whom they can contact with questions or concerns about the program or their future career path–the idea being that these mentors can continue to encourage the students to



>> *Rural physician recruitment and retention*

for rural physicians

pursue rural careers. "For the 2002–2003 school year, we have matched 11 students with faculty advisors who work in a rural setting," says Dr. Rowntree.

Part three of the study will involve a follow-up questionnaire as students enter their second year of medical school in 2003. This survey will evaluate the students' experiences with their mentors and determine whether the students are still interested in rural careers. The timing of the second survey is based on the fact that U of C has a three-year Medicine program and students must make decisions about what sort of residency to do early in their third year.

Dr. Rowntree hopes that the results of her study can be used to set up programs to encourage more students to become rural physicians. She points out that in Canada, some medical schools are considering altering their admissions policies to encourage students who may be interested in rural careers. A large scholarship program aiming to attract rural kids to medical school and other health professions already exists in Australia. In northern Ontario, a new medical school aimed at easing the chronic doctor shortages in the province's rural areas will open in September 2004.

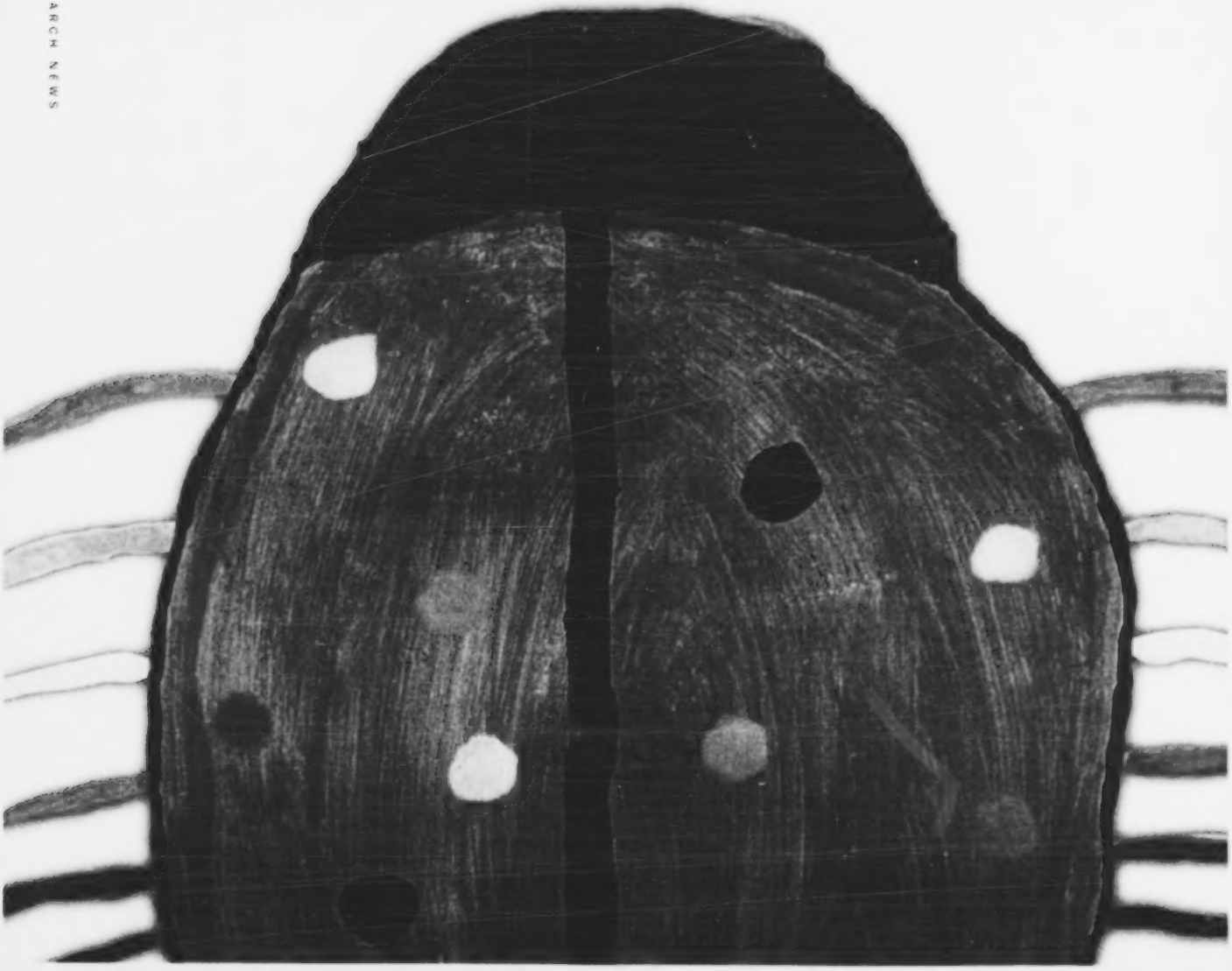
"Traditionally, we have solved our rural physician shortages in Canada by recruiting doctors from other nations," says Dr. Rowntree. "But for a privileged nation to recruit doctors from developing countries only serves to worsen the shortages of skilled healthcare workers in those countries and raises a few ethical questions. Maybe we should be focusing on finding the Dr. McCoys in our own backyard."

The SEARCH program is delivered through a multidisciplinary team from the University of Alberta and University of Calgary faculties of nursing, medicine, and business. Sharon Matthias of Matthias Inc. is the mentor for Dr. Rowntree's project and is one of three SEARCH faculty team leaders, along with Dr. Ann Casebeer, Assistant Professor in the U of C Department of Community Health Sciences, and Dr. Robert Hayward, Director of the Centres for Health Evidence at the U of A. SEARCH is one initiative of AHFMR's Applied Health Research Programs.

SEARCH

ABOVE: DR. CAROL ROWNTREE

New tools in the fight against cancer



"This is a pivotal time in cancer research. I've felt an excitement in the past five years that I haven't experienced in the prior 20 years."

Alberta's Dr. Tony Fields knows what he's talking about. His career has been dedicated to developing strategies for fighting cancer in Canada, most recently as the president of the National Cancer Institute of Canada, the largest charitable funder of cancer research in Canada. Albertans might be more familiar with Dr. Fields as the Alberta Cancer Board's vice-president of Medical Affairs and Community Oncology, and as the former director of the Cross Cancer Institute in Edmonton.

"Researchers have made fundamental discoveries in genetics, molecular biology, and cellular biology, and we're now at the stage where this knowledge is being transformed into tools we can apply to treat cancer more effectively. We're seeing results such as age-standardized mortality rates for many cancers going down."

This decrease is an important point, Dr. Fields points out. He notes that reports in the media tend to focus on the rising incidence of cancer. Indeed, if current trends continue, the incidence of cancer in Canada could increase by as much as 70% over the next 15 years. But this increase is predominantly due to population growth and aging, not an increased individual risk of cancer. There are more people in the country; therefore, more people will get cancer. And because our population is aging and cancer is primarily a disease of older people, cancer incidence is on the rise.

"So while cancer incidence rates clearly show the growing need for effective care for Canadians who develop cancer, and are a sober reminder that we must pay more attention to prevention, the age-standardized mortality rates do not support a doom-and-gloom outlook on cancer," Dr. Fields emphasizes. "Instead, they point to the effectiveness of cancer research. I lived through the days when there was only one chemotherapy drug for colorectal cancer. Now we have two additional drugs that are proven advances, and several promising new agents in clinical trials. Research is making a difference."

The Alberta Heritage Foundation for Medical Research provides regional funding for cancer-related research in Alberta. Since 1980, AHFMR has contributed approximately $30 million to cancer research and has supported more than 40 senior investigators and 190 trainees in this field. "AHFMR is a regional foundation that has made a significant impact on the Canadian cancer research scene," says Dr. Fields.

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DR. TONY FIELDS

Profiling cancer

One of the areas of cancer research that has progressed rapidly in the past 10 years is molecular profiling. Traditionally, cancers are classified by their site of origin in the body as well as their appearance under the microscope. Now, because we understand much more about the molecular changes in cells that cause cancer, researchers are developing methods to identify these molecular changes.

Molecular profiling is expected to have great value in more accurately determining how best to treat cancer patients. It has already resulted in the development of new cancer therapies. The drug Herceptin (trastuzumab), now approved for use in Canada, was developed as a breast cancer treatment for women who have a greater-than-normal number of copies of a gene called HER2. This overexpression of HER2 occurs in approximately 25% of breast cancer patients and can result in a more aggressive form of the disease. Herceptin works by specifically targeting tumor cells that overexpress the HER2 protein.

"There's still a lot of work that needs to be done before molecular profiling becomes widely used," says Heritage Senior Scholar Dr. Stephen Robbins. "The technology to do profiling in an efficient way is very new. Our facility in Calgary, the Southern Alberta Microarray Facility, is only the third site in Canada to have this technology. Before we had this equipment, we had the capability to study 10 to 20 genes at one time. Now we can examine 20,000 genes—the genetic makeup of a person—on one slide.

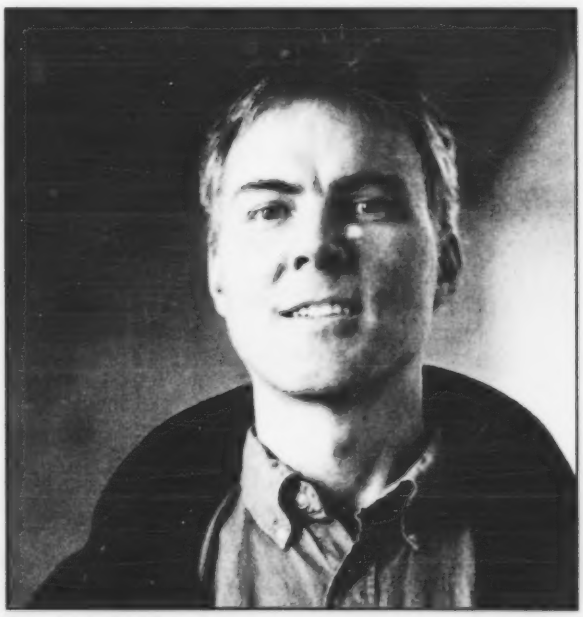
"Now we can examine 20,000 genes—the genetic makeup of a person—on one slide."

"But technology is only part of molecular profiling. We also need to collect data on the relative expression of each gene for many, many people before we can draw conclusions about a molecular profile for a particular type of cancer."

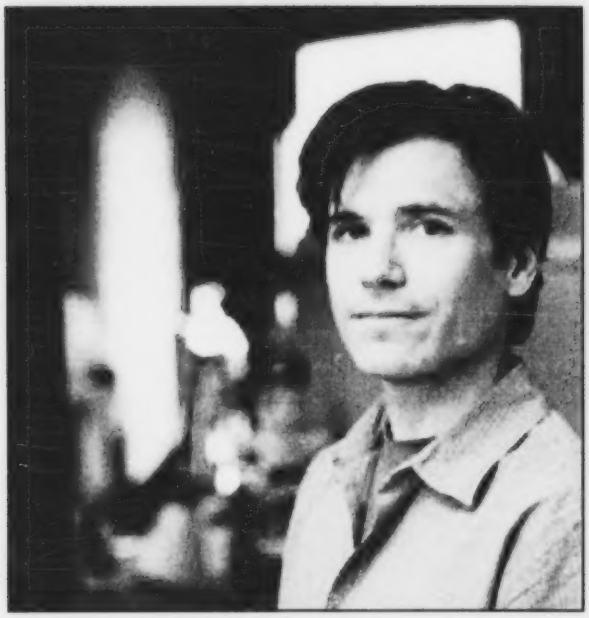
The Southern Alberta Microarray Facility, located at the University of Calgary, serves researchers from across the province. One of the projects at the facility is focused on Wilms' tumour, a type of childhood kidney cancer. The research is a collaborative effort between the University of Calgary and the University of Alberta, which has the largest bank of Wilms' tumours in the world.

Conventional therapy for Wilms'—usually a combination of surgery with chemotherapy and/or radiation—is very successful, curing about 85% of patients. "However, 15% of patients will relapse," says Dr. Robbins. "We don't know why. It's possible that all these patients require is more aggressive therapy. But with an 85% cure rate, you can't ethically expose so many children to a therapy they're not likely to need. If you knew the molecular profile of tumours that are likely to relapse, you could offer aggressive therapy only to those patients. This is the promise of molecular profiling."

At the University of Alberta, Heritage Scholar Dr. Mark Glover is looking at a different kind of molecular profiling for two genes that are linked to hereditary breast cancer. Mutations in these genes, called BRCA1 and BRCA2, cause early-onset breast cancer and account for 5% to 10% of all breast cancer cases.



DR. STEPHEN ROBBINS



"When more is known about a certain type of cancer, patients can make better-informed decisions about therapy."

"The problem is that we don't know exactly which mutations in BRCA1 and BRCA2 will cause cancer," explains Dr. Glover. "Genes have many irregularities (we call them natural polymorphisms), as well as mutations that cause cancer."

Dr. Glover's lab studies the protein made by the BRCA1 gene. It's a huge protein—1863 amino acids long. His team is looking at the C terminus, a segment only 250 amino acids long, where mutations tend to cluster. There are 80 to 100 different kinds of mutation in this segment.

"We're evaluating the ones that are likely to cause cancer," says Dr. Glover. "Part of the work involves determining the three-dimensional structure of the mutated protein segment. If a mutation disrupts the 3-D structure of the protein, I feel confident in saying that it's a cancer-causing mutation.

"Clinicians want to know this information. When more is known about a certain type of cancer, patients can make better-informed decisions about therapy."

Putting molecular information about cancer in the hands of the doctors who are treating patients is the goal of research involving engineering and medical researchers from the Alberta Cancer Board, the University of Alberta, and the University of Calgary. The team, headed by U of A researchers Dr. Linda Pilarski and Dr. Chris Backhouse, along with Dr. Karan Kaler at the U of C, is developing a lab-on-a-chip to assess the genetic makeup of cancer cells from a biopsy.

"This is the kind of information you can't get from looking at a slide of cancer cells in a microscope," explains Dr. Pilarski, an oncology researcher at the University of Alberta and the Cross Cancer Institute. "To determine genetic makeup, you need molecular tests that are currently done in specialized laboratories with high-tech equipment. They are time-consuming and expensive."

Dr. Pilarski's group believes that nanotechnology holds the key to developing a fast and inexpensive way to identify genetic makeup. Their lab-on-a-chip is envisioned as a little platform about the size of a microscope slide that would search for a certain set

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ABOVE: DR. MARK GLOVER

DR. LINDA PILARSKI

"Nanotechnology holds the promise of making this device cheap, automated, and standardized."

of diagnostic genes, depending on the type of cancer. The results would come up on a computer screen, summarizing any genetic abnormalities for the doctor and perhaps even suggesting treatment.

"Nanotechnology holds the promise of making this device cheap, automated, and standardized," explains Dr. Pilarski. "The results would be the same whether the test is done at Harvard or in Tuktoyaktuk. The routine genetic characterization of cancers would make possible the customized treatment of cancer, which would maximize the chance of success and minimize side effects."

Understanding pathways

The gene mutations Dr. Pilarski's team is looking for are the ones which disrupt the intricate mechanisms of signalling and control that underlie the normal functioning of a cell. Many scientists are attempting to understand these carefully choreographed series of events. By doing so, they hope to uncover what goes wrong to cause cancer, and thus find a potential target for new drugs.

Learning more about complex molecular pathways is the focus of research done by Heritage Scientist Dr. Don Fujita from the University of Calgary. He has spent more than 15 years teasing out the secrets of the c-Src protein and the c-src gene that makes it. His lab, in collaboration with Dr. H. J. Kung, now of the University of California Davis Medical Centre, was the first to clone and sequence the human cellular src gene, and to determine the amino acid sequence of the human Src protein. Growth and development in many normal cells depend on the action of the Src protein. "But when mutated or abnormally activated, we think that Src has the potential to become a powerful cancer-causing agent," Dr. Fujita explains.

The gene makes a protein that is an important player in several signalling pathways that control various important cellular functions. For example,

Research shows that Src is activated in breast, colon, ovarian, and pancreatic cancers, among others.

Src is involved in the control of cell proliferation (reproduction), and in stimulating the growth and function of blood vessels. "But when some mechanism turns up the activity of the Src protein to a very high level, the result can be uncontrolled cell proliferation, tumour formation, blood vessel growth (angiogenesis), and tumour metastasis," Dr. Fujita says. Research shows that Src is activated in breast, colon, ovarian, and pancreatic cancers, among others.

Dr. Fujita's laboratory has found that in many breast cancer cells Src is activated to unusually high levels, and that high levels of another protein in these cells (called PTP1B) could be involved in activating Src. In metastatic colon cancer, research has shown that Src is activated through another mechanism: mutation. A collaboration with Dr. Tim Yeatman of the University of South Florida

ABOVE: DR. DON FUJITA

led to the discovery of the first such activating mutation of Src found in a human cancer.

"We've been studying the regulation of Src and how it is activated, as well as some of the important cellular signalling pathways that Src is involved in," says Dr. Fujita. "I believe that a better understanding of the molecular events and pathways that involve Src and other potentially oncogenic proteins is one of our best hopes for the future development of drugs or molecules that are highly specific and effective against cancer cells."

At the University of Alberta, Heritage Clinical Investigator Dr. Charlie Hao is studying yet another pathway: programmed cell death (apoptosis). "Most cells are programmed to die naturally at some point in time," he explains, "but in cancer this process is essentially turned off, so that cancer cells proliferate and do not die. Cancer cells still have the program for death, but it has been hijacked by the proliferation pathway. We need to change the signal pathways."

Dr. Hao has had success with a protein known as TRAIL, using it to induce programmed cell death in brain cancer (malignant glioma) and skin cancer (malignant melanoma) cells. Using certain chemotherapeutic drugs, his team can switch cancer cells from a proliferation to a programmed cell death pathway so that TRAIL can kill 70% of 25 cell lines for each cancer type established in the laboratory. The drugs can also kill the cancer cells taken directly from patients.

"In order to develop truly effective cancer therapies, we must understand these mechanisms."

"Our next step is to develop a clinical approach so that TRAIL can be used on patients, either alone or in combination with chemotherapeutic drugs," says Dr. Hao. To prepare for clinical trials, he has looked at possible side effects of TRAIL on human livers. This work, done in collaboration with U of A Heritage researcher Dr. Norman Kneteman, and colleagues Dr. Lorne Tyrrell and Dr. Kenneth Petruk, has shown that TRAIL is not toxic to normal human cells in culture or in animals. "We're still at the early stages," Dr. Hao notes, "but I believe that in order to develop truly effective cancer therapies, we must understand these mechanisms that regulate cancer cell death and growth. This will take time."

Heritage Senior Scholar Dr. Jim Stone knows all about patience. In 1984, he began studying the Ras pathway, which controls cell growth and division. Sixteen years later his work, in collaboration with his colleagues at the University of Alberta, led to the discovery of a molecule that could lead to new ways of treating cancer.

The Ras pathway is important because a single mutation of the Ras gene can lead to the formation of an oncogene (a gene that induces or promotes uncontrolled cell growth) and a cancer-causing Ras protein. About 90% of pancreatic cancers, 30% of lung and colorectal cancers, and 24% of acute myeloid leukemias harbour Ras mutations.

Dr. Stone's team discovered a protein called RasGRP that interacts with Ras, and has the same effect on the Ras pathway as a mutation in the Ras gene itself. "So we wanted to know what regulates RasGRP. Much to our surprise, we found it was a

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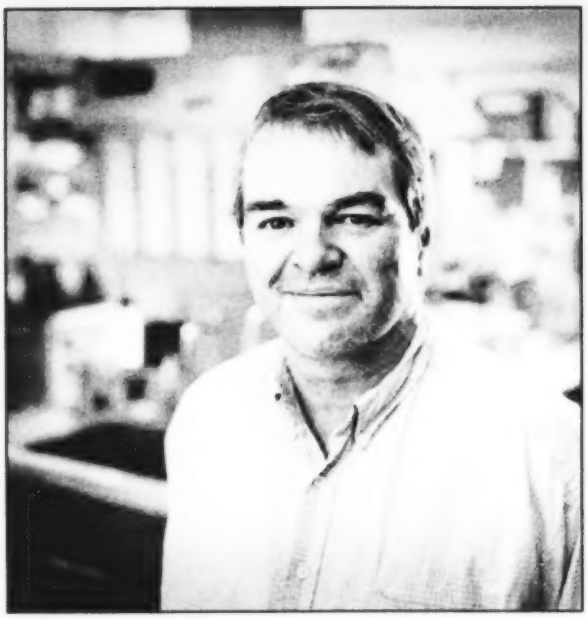
DR. CHARLIE HAO



"Cancer research takes an incredible amount of time and is technically very challenging."

particular lipid called diacylglycerol. We think when this lipid amasses in the cell, RasGRP becomes activated."

This discovery has led Dr. Stone to hypothesize that leukemia and lymphoma (both blood-related cancers) are diseases of lipid metabolism. He recently received a three-year grant from the Alberta Cancer Board to test this novel hypothesis. It's not going to be easy because there are many different types of leukemia and lymphoma and Dr. Stone must find tumours in which RasGRP is expressed.

"Cancer research takes an incredible amount of time and is technically very challenging," he says. "For example, simply making a good antibody can take six months to a year, and only then can you start the experiment. I'd say that 99% of the work we do involves being meticulous and careful so you can put yourself in the position to do something original, something that makes a real difference."

And making a difference is what cancer research is all about, says the National Cancer Institute of Canada's Dr. Tony Fields, who introduced this story. He contends that what is needed now is an emphasis on translational research–research that translates the discoveries of basic science into benefits to people, such as new or improved therapies.

"There's a bottleneck in the path from biological discovery to clinical application," Dr. Fields says. "The wheels of discovery are spinning fast, the wheels of translation are moving more slowly. But we are beginning to pay attention to this issue, and it will go a long way to reducing the burden of cancer for Canadians."

Dr. Tony Fields is president of the National Cancer Institute of Canada and vice-president of Medical Affairs and Community Oncology at the Alberta Cancer Board.

Dr. Stephen Robbins is an Associate Professor in the departments of Oncology and Biochemistry & Molecular Biology at the University of Calgary, as well as director of the Southern Alberta Microarray Facility. He is an AHFMR Senior Scholar; his research is also funded by the Canadian Institutes of Health Research (CIHR), the Cancer Research Society, and the Kids Cancer Care Foundation of Alberta.

Dr. Mark Glover is an Associate Professor in the Department of Biochemistry at the University of Alberta. He is an AHFMR Senior Scholar and a CIHR Investigator, and holds a Canada Research Chair in Structural Molecular Biology. His research is also supported by the Canadian Breast Cancer Research Initiative, in partnership with the National Cancer Institute of Canada (NCIC).

Dr. Linda Pilarski is a Professor in the Department of Oncology at the University of Alberta and a Senior Scientist at the Cross Cancer Institute (Alberta Cancer Board). Her research is supported by CIHR; NCIC; NIH (National Institutes of Health); and NSERC (Natural Sciences and Engineering Research Council of Canada).

Dr. Don Fujita is a Professor in the Department of Biochemistry and Molecular Biology at the University of Calgary and a member of the Cancer Biology Research Group. An AHFMR Scientist, he also receives funding from

ABOVE: DR. JIM STONE

the U.S. Department of Defense Breast Cancer Program; the Canadian Breast Cancer Foundation, AB/NWT Chapter; and the Alberta Cancer Board.

Dr Chunhai (Charlie) Hao is an Associate Professor and neuropathologist in the Department of Laboratory Medicine and Pathology at the University of Alberta. He is an AHFMR Clinical Investigator; his research is also supported by CIHR and the University Hospital Foundation.

Dr. Norm Kneteman is a Heritage Senior Scholar and a Professor in the University of Alberta Department of Surgery.

Dr. Jim Stone is an Associate Professor in the Department of Biochemistry at the University of Alberta. An AHFMR Senior Scholar, he receives additional research support from CIHR, NCIC, and the Alberta Cancer Board.

Selected publications

Arcellana-Panlilio M, Robbins SM. Cutting-edge technology: I. global gene expression profiling using DNA microarrays. *American Journal of Physiology - Gastrointestinal and Liver Physiology* 2002 Mar;282(3):G397-G402.

Williams RS, Green R, Glover JNM. Crystal structure of the BRCT repeat region from the breast cancer-associated protein BRCA1. *Nature Structural Biology* 2001 Oct;8(10):838-842.

Keate JJ, Reiman T, Maxwell CA, Taylor BJ, Larratt LM, Mant MJ, Belch AR, Pilarski LM. In multiple myeloma, t(4;14)(p16;q32) is an adverse prognostic factor irrespective of FGFR3 expression. *Blood* 2003 Feb 15;101(4):1520-1529.

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Dower NA, Stang SL, Bottorff DA, Ebinu JO, Dickie P, Ostergaard HL, Stone JC. RasGRP is essential for mouse thymocyte differentiation and TCR signaling. *Nature Immunology* 2000 Oct 1;1(4):317-321.

The different pathways to endometrial cancer

"We are looking to go beyond the current classification scheme for endometrial cancer, which has two main subtypes," explains Dr. Cook. "We've used advanced molecular biology tools to propose a new classification scheme with five subtypes."

The researchers are interested in determining what risk factors play a role in each subtype. Risk factors include early menstruation, late menopause, and hormone replacement therapy. Because this pilot project is part of a much larger case-control study of endometrial cancer, the researchers will also be able to look at lifestyle factors and lifetime physical activity patterns.

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"We propose that there are different pathways to endometrial cancer," says Dr. Cook, "so we expect that risk factors will differ for the specific subtypes of endometrial cancer. We want to clarify these relationships, which might one day lead to better prevention, diagnosis, and treatment."

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Williams RS, Green R, Glover JNM. Crystal structure of the BRCT repeat region from the breast cancer-associated protein BRCA1. *Nature Structural Biology* 2001 Oct;8(10):838-842.

Keate JJ, Reiman T, Maxwell CA, Taylor BJ, Larratt LM, Mant MJ, Belch AR, Pilarski LM. In multiple myeloma, t(4;14)(p16;q32) is an adverse prognostic factor irrespective of FGFR3 expression. *Blood* 2003 Feb 15;101(4):1520-1529.

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The different pathways to endometrial cancer

Heritage Scholar Dr. Linda Cook is bringing an epidemiologist's perspective to the molecular profiling of cancer. Working with University of Calgary colleagues Dr. Anthony Magliocco and Dr. Christine Friedenreich, she is heading a pilot project to develop tissue and serum markers for endometrial cancer. It is the most common cancer originating in women's reproductive organs, and the fourth most common cancer in Canadian women. The disease normally occurs in post-menopausal women and is often caught early because it usually triggers abnormal bleeding. The prognosis is good after a hysterectomy.

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ABOVE: DR. LINDA COOK

Dr. Linda Cook is an Associate Professor in the Department of Community Health Sciences at the University of Calgary. An AHFMR Health Scholar and a Research Scientist at the Alberta Cancer Board, Dr. Cook is also supported by the Canadian Institutes of Health Research (CIHR), the National Cancer Institute of Canada (NCIC), and Alberta's M.S.I. Foundation.

Selected publication

Kmet LM, Cook LS, Magliocco AM. A review of p53 expression and mutation in human benign, low malignant potential, and invasive epithelial ovarian tumours. *Cancer* 2003 Jan;97(2):389-404.

This insight led Dr. Gainer to work on immune therapies for cancer.

"We took a novel approach, using a gene gun for gene therapy. It worked modestly well," says Dr. Gainer. "But as I got further and further into it, I could see how incredibly complex the immune system is. It is very difficult to turn it off because of all the overlapping pathways. It occurred to me that it would be much easier, and probably more clinically successful, to turn it on."

This insight led Dr. Gainer to work on immune therapies for cancer. Now a Heritage Clinical Investigator at the University of Alberta's Surgical-Medical Research Institute, her research focuses on developing a vaccine that increases the visibility and susceptibility of brain tumour cells, making them more sensitive to a patient's own immune system.

Surgery is the first line of attack for malignant brain tumours. "While surgeons can remove the bulk of the tumour, they rarely get all the cancer cells," explains Dr. Gainer. "Thus, we need another way to kill the remaining cells."

The idea behind a cancer vaccine is to make the immune system capable of effectively fighting the cancer on its own. Dr. Gainer's focus is on dendritic cells, which are a key part of the immune system. They act as sentries throughout the body, looking for signals indicative of infection or disease. When they find something, they take a sample back to the lymph node, to help them locate the correct T cell that can recognize and fight the disease. Currently, Dr. Gainer grows dendritic cells from stem cells harvested from cord blood samples, which are obtained when a baby is delivered. (These are not embryonic stem cells, currently the subject of much controversy.)

Differentiating stem cells and extensively characterizing the resulting dendritic cells has been a lengthy challenge for Dr. Gainer's lab. Now that they have passed this hurdle, work on developing a vaccine can continue. Although the research is in its early stages, Dr. Gainer envisions eventually preparing a vaccine by harvesting a patient's own stem cells, differentiating them into dendritic cells, and exposing them to the patient's tumour cells. When they are administered back to the patient, these dendritic cells would produce a strong immune response to the cancer.

Dr. Anita Gainer is an Assistant Professor in the Surgical-Medical Research Institute at the University of Alberta, and an AHFMR Clinical Investigator.

Selected publication

Gainer AL, Young ATL, Parney IF, Petruk KC, Elliott JF. Gene gun transfection of human glioma and melanoma cell lines with genes encoding human IL-12 and GM-CSF. *Journal of Neuro-Oncology* 2000 Mar;47(1):23-30.

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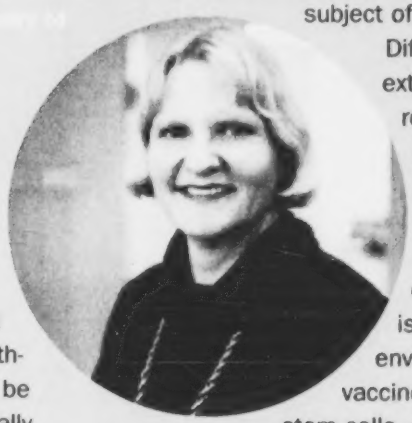

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Selected publication

Gainer AL, Young ATL, Parney IF, Petruk KC, Elliott JF. Gene gun transfection of human glioma and melanoma cell lines with genes encoding human IL-12 and GM-CSF. *Journal of Neuro-Oncology* 2000 Mar;47(1):23-30.

Complementary cancer therapies

When faced with a diagnosis of cancer, many people seek out treatment in addition to the conventional therapy (surgery, radiation, chemotherapy) prescribed by their doctors. Complementary therapies run the gamut from special diets and vitamins, through yoga and meditation, to treatments such as acupuncture and massage. Some of these are intended to help battle the cancer, while others are designed to relieve discomfort or improve quality of life. Although there is scientific evidence for the effectiveness and safety of some complementary therapies, many have not been scientifically tested.

How do patients make a decision about using complementary therapies?

So how do patients make a decision about using complementary therapies? What kind of information is important to them? These questions are being asked by the University of Calgary's Dr. Marja Verhoef in an innovative study supported by the Health Research Fund, which is administered by AHFMR.

"Cancer patients are choosing complementary therapies in ever-increasing numbers," says Dr. Verhoef. "Cancer information lines are swamped with requests for information about these therapies. Not only do we have little information to offer patients right now, but we also don't know what patients perceive evidence to be, how important evidence is to them, and how they wish to receive information on complementary therapies."

Dr. Verhoef's research will assess cancer patients' understanding of evidence, the role scientific evidence plays in evaluating complementary medicine, and of complementary therapies themselves. The first part of the study, which involves in-depth interviews with cancer patients in Vancouver and Calgary, is underway now. The themes arising from the interviews will be used to design a questionnaire to be administered to 400 cancer patients in southern Alberta and 250 callers to the Canadian Cancer Society's Cancer Information Service.

"The prevalence of cancer is not decreasing, and many people now live with cancer for many years. So quality of life issues become very important, and patients search for treatments that will help them," notes Dr. Verhoef. "We need to pay attention to these issues. If caregivers knew more about how patients make decisions about complementary therapies, what they consider important, it would help them provide the information patients need, as well as provide it in the way they need it."

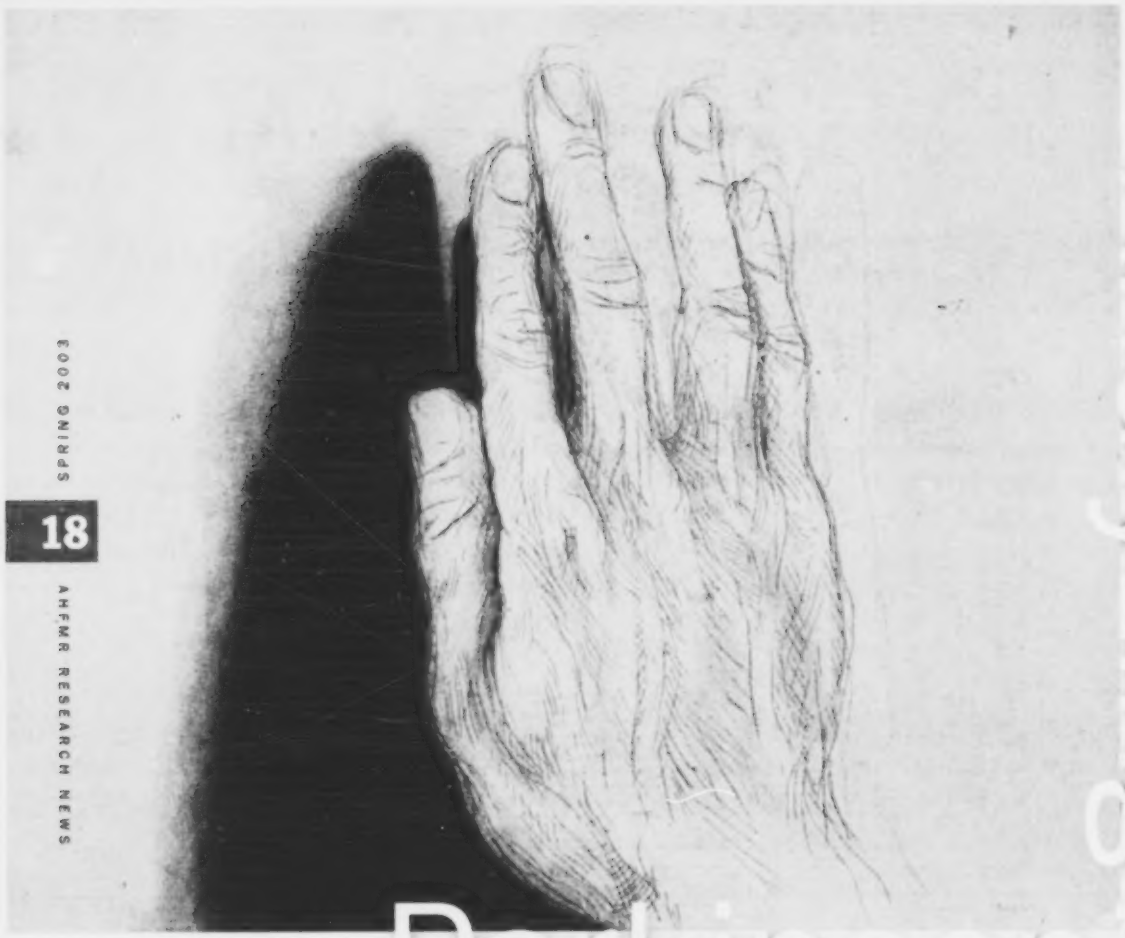
RIGHT: DR. MARJA VERHOEF

Dr. Marja Verhoef is a Professor in the Department of Community Health Sciences at the University of Calgary and a Canada Research Chair in Complementary Medicine.

She receives support for her study from the Health Research Fund, administered by AHFMR on behalf of Alberta Health and Wellness, as well as from Health Canada and the National Cancer Institute of Canada. Dr. Verhoef is also a faculty member for AHFMR's SEARCH program.

Selected publication

Verhoef MJ, Casebeer AL, Hilsden RJ. Assessing efficacy of complementary medicine: adding qualitative research methods to the "gold standard". *Journal of Alternative and Complementary Medicine* 2002 Jun;8(3):275-281.



Analyzing Parkinson's

"By 2020 the number of cases of the disease is expected to triple."

If you visited the office of Heritage Scholar Dr. Gerlinde Metz, you might be invited to help yourself to a tin of Swiss chocolates on her desk. The resulting fine-motor movements necessary to grasp, unwrap, and place one of the chocolates in your mouth are the sort of movements that can become difficult for a person afflicted with Parkinson's disease—the focus of Dr. Metz's research at the University of Lethbridge's Canadian Centre for Behavioural Neuroscience (CCBN).

Parkinson's is a slow, progressive disease of the central nervous system that is characterized by shakiness, rigidity, and loss of balance—motor symptoms which can lead to major disability. "Someone suffering from Parkinson's might be unable to write or to button their clothing," Dr. Metz explains. As the disease progresses, there may also be cognitive symptoms such as dementia, as well as deficits in language and attention.

The disease is caused by the death of cells in one area of the brain that controls motor function. Dr. Metz points out that these cells die gradually as we age, but that with Parkinson's, this cell loss is accelerated. Health Canada estimates that one in every 100 Canadians over the age of 60 will be diagnosed with the disease.

"With Canada's aging population, we are seeing 5,000 more cases of Parkinson's disease each year," says Dr. Metz. "Yet incidence of Parkinson's in younger people is also increasing. By 2020 the number of cases of the disease is expected to triple. You can see why it is so important for us to learn more about the factors involved."

ARTWORK: ERNESTO BONATO, *UNTITLED (HAND)*, 2000. ETCHING ON PAPER 22/25, 21.5 X 25.4CM. COLLECTION OF THE ALBERTA FOUNDATION FOR THE ARTS.

Prolonged or frequent exposure to pesticides or other environmental factors is one of the conditions thought to be connected to the increased incidence of Parkinson's in younger people. As an example, Dr. Metz points to actor Michael J. Fox, who was diagnosed with the disease at the age of 30. Recently, it has been suggested that Fox's exposure in the mid-1970s to certain toxins on the set of a CBC sitcom in which he starred may have contributed to the disease. Alberta has a high incidence of Parkinson's compared to other provinces, and our extensive rural areas where pesticides are in use could be a contributing factor.

Alberta has a high incidence of Parkinson's compared to other provinces.

Dr. Metz is focusing many of her experiments on the role stress plays in the disease, something which has not previously been investigated. Triggered by such everyday activities as driving in heavy traffic, struggling to meet a work deadline, or juggling the demands of family life, stress can cause an increase in heart rate, blood pressure, respiration, metabolism, and adrenaline level, as well as a decrease in appetite.

"With the lifestyles that we lead today, it seems obvious that stress might have an effect in this disease," Dr. Metz explains. "It certainly changes how the brain works; for instance, it changes how we learn. But we don't know how stress changes how we move." Dr. Metz and her colleagues at the CCBN have developed a variety of tests to measure these changes in movements. They are also trying to distinguish between compensation and recovery after therapy: Compensation means that the subject finds a new way to adapt a particular movement to accomplish the same task; recovery is regaining the movement.

While Dr. Metz hopes the knowledge she gains may someday be used to develop new treatments for Parkinson's, part of her current research focus is to test existing therapies. She explains that all treatments for the disease seem to work for a period of time and then become less efficient. They also do not halt the ongoing cell loss, so the disease continues to progress and symptoms get worse. Levodopa, for instance, currently the only standard treatment for Parkinson's, replaces the dopamine (a chemical messenger in the central nervous system) lost when the cells die, but really only treats the symptoms of the disease. "If we know what the factors are that cause this disease, maybe we can find ways to slow down or even stop the disease," says Dr. Metz.

A behavioural biologist by training, Dr. Metz's interest in motor-system functions was piqued in Zurich, Switzerland, where she completed a doctorate at the Swiss Federal Institute of Technology. She came to Lethbridge to do post-doctoral work with fellow CCBN investigator Dr. Ian Whishaw and has now been in the city for three and a half years.

"This is the very best place to do this kind of analysis," she says of the Centre.

DR. GERLINDE METZ

Dr. Gerlinde Metz is an Assistant Professor in the Department of Psychology and Neuroscience at the University of Lethbridge. She is a Heritage Scholar and also receives funding from the NIH (National Institutes of Health).

AHFMR contributed $1.65 million in funding toward the Canadian Centre for Behavioural Neuroscience at the University of Lethbridge.

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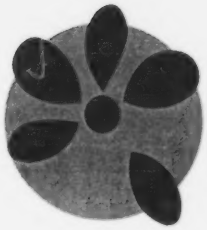
Medical physics and ovarian cancer

Alasdair Syme coaches women's hockey in his spare time. While his players are undoubtedly grateful for the effort he puts into coaching their team, someday some of them may be even more grateful for the University of Alberta Ph.D. candidate's cutting-edge research work. Alasdair specializes in medical physics, which uses radiation to diagnose and treat cancer, and is working with a group of U of A researchers to find a better treatment for late-stage ovarian cancer.

ALASDAIR SYME

Ovarian cancer has one of the worst prognoses of all cancers because it is often discovered too late to be treated effectively. The usual course of treatment involves surgery and chemotherapy, but these can leave bits of cancerous tissue still floating in the fluid bathing the abdominal cavity, or tumour nodules embedded on surfaces within the cavity. If these aren't removed or destroyed, the cancer could spread to other organs in the abdomen.

The U of A's radiopharmacy group is trying to develop a treatment that involves injecting immunoliposomes—laboratory-created molecules which have been tagged with a radioactive substance—into the abdominal cavity where they would seek out and bind to the stray cancer cells. Ideally, the radiation would be given in doses that would be toxic only to the cancerous cells, thus sparing healthy surrounding tissue. Alasdair is using mathematical modelling to figure out how many of the targeting molecules actually bind to the cancerous cells and how much of the radioactive substance is needed to destroy the cells while minimizing damage to healthy tissue.



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The group is using the radioisotope rhenium-188 to tag to the immunoliposomes because it has a half-life of only 17 hours. It decays significantly and becomes less dangerous to healthy tissue before the immunoliposomes escape from the abdominal cavity to other parts of the body. In addition, rhenium-188 emits the ideal level of particle energy for the therapy.

Alasdair came to the U of A in 1999, after completing his honours B.Sc. at McMaster University in Hamilton. He has been working on his current research for almost two years and likes dealing with something that has real-world applications. "A lot of people who go into physics are interested in pure research, and I guess I'm just not that way," he says. "I like the idea of some applicability to my research. Medical physics seemed ideal for that, especially when you're dealing with something like cancer therapy."

Alasdair's work is an important component of the research being done by the university's radiopharmacy group, says graduate supervisor Dr. Steve McQuarrie, a U of A Associate Professor of Pharmacy and Pharmaceutical Sciences. He expects trials of the therapy to begin this spring, and if the results look good, human studies could start in two years.

Alasdair Syme, a Ph.D. candidate in physics at the University of Alberta, holds an AHFMR Studentship and also receives funding from NSERC.

In December 2002, the University of Alberta Medical Physics graduate program became only the second of its kind in Canada to be accredited by the Commission on Accreditation of Medical Physics Educational Programs.

Selected publication

Syme A, McQuarrie SA, Fallone BG. Beta dose-rate distributions in microscopic spherical tumours for intraperitoneal radioimmunotherapy. *International Journal of Radiation Oncology Biology Physics*. In Press.

reader resources

Closing the gate on pain

Neuromed Technologies Inc.
http://www.neuromedtech.com/main.htm

Eliminating copycats

Dr. Kenneth Ng's web sites
http://www.ucalgary.ca/~ngk
http://www.ucalgary.ca/SC/BI/biochem/ng.html

Biotech: The fire in the belly

Biomira
http://www.biomira.com

The SEARCH for rural physicians

SEARCH web site
http://www.ahfmr.ab.ca/search.shtml

Alberta Rural Physician Action Plan
http://www.roap.ab.ca

New tools in the fight against cancer

Canadian Cancer Statistics 2002
http://www.hc-sc.gc.ca/pphb-dgspsp/publicat/ccs-sce02

Canadian Cancer Society
http://www.cancer.ca

National Cancer Institute of Canada
http://www.ncic.cancer.ca

Alberta Cancer Board
http://www.cancerboard.ab.ca

Dr. Stephen Robbins's web site
http://www.robbinslab.com

Dr. Mark Glover's web site
http://gloverlab.biochem.ualberta.ca

Complementary cancer therapies

Canada Research Chairs
http://www.chairs.gc.ca

Analyzing Parkinson's

University of Lethbridge Canadian Centre for Behavioural Neuroscience
http://ccbn.uleth.ca

Medical physics and ovarian cancer

University of Alberta Division of Medical Physics
http://med.phys.ualberta.ca/medphys/

AHFMR announces $27.5 million for health research

Can we predict sudden cardiac death? Are there ways to intervene? At the University of Calgary, Heritage researcher Dr. Anne Gillis is trying to answer these questions through her study of the regulation of heart rate and rhythm. Her research has already led to refinements in pacemakers and implantable defibrillators, which have improved the quality of life for countless heart patients.

Dr. Gillis has been offered an Alberta Heritage Foundation for Medical Research (AHFMR) Scientist award, the highest award possible from the Foundation. She is the first physician-researcher recruited to Alberta as a Heritage Clinical Investigator to attain this prestigious level of funding. Funded by AHFMR for a total of 17 years, she maintains an active clinical practice in addition to conducting cardiac research.

Dr. Gillis is one of 43 scientists offered a total of $27.5 million in funding from AHFMR in the 2003 competition. Also included in this year's awards is University of Calgary researcher Dr. Daniel Lai, who examines multicultural health issues in the aging population. Dr. Lai has become AHFMR's first-ever awardee in the Faculty of Social Work. At the University of Alberta, 2003 Heritage awardees include Dr. Karin Olson who studies cancer-related fatigue in palliative care patients, and Dr. John Greer who investigates the formation of the nerves and muscles which control breathing in the developing fetus.

With the implementation of the new awards, AHFMR will be funding 250 senior Alberta-based researchers working in a variety of faculties at the province's three main universities. The 2003 awards bring the total amount contributed by AHFMR to Alberta's medical research community to more than $750 million.

Applications for AHFMR's senior personnel awards are peer-reviewed by scientists from around the world, ranked by a scientific advisory committee, and finally approved by the AHFMR Board of Trustees. Researchers must meet the very highest international standards of excellence in order to receive Heritage funding—a process which continues to build a world-class community of health researchers in Alberta.

For a complete list of AHFMR's 2003 Senior Personnel Awards go to: http://www.ahfmr.ab.ca

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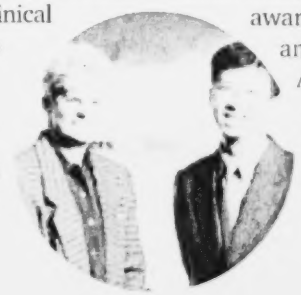

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